Search Strategy

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     FILE 'USPATFULL' ENTERED AT 16:54:21 ON 09 DEC 2003

                  E KENT STEPHEN/IN
L34            39 S E4 OR E5
                  E RAMSHAW I A/IN
L35             3 S E4
                  E BOYLE DAVID B/IN
L36             4 S E3 OR E4
L37             2 S L36 NOT L35

     FILE 'WPIDS' ENTERED AT 17:14:58 ON 09 DEC 2003

                  E KENT STEPHEN/IN
                  E RAMSHAW IAN A/IN
L38             7 S E2
                  E BOYLE D B/IN
L39            37 S E3

     FILE 'MEDLINE' ENTERED AT 17:17:26 ON 09 DEC 2003

                  E RAMSHAW I A/AU
L40            94 S E3-E5
L41            82 S L40 AND PY<2000

     FILE 'MEDLINE' ENTERED AT 18:06:05 ON 09 DEC 2003
                  E RAMSHAW I A/AU
L1             91 S E3 OR E4
L2             79 S L1 AND PY<1999
L3              0 S L2 AND (FPV OR FOWL POX VIRUS)
L4              0 S L2 AND AVIPOX
L5              0 S L2 AND (GAG OR POL)
L6              3 S L2 AND (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L7             29 S L2 AND (CYTOKINE? OR INTERLEUKIN? OR INTERFERON?)

     FILE 'USPATFULL' ENTERED AT 18:19:22 ON 09 DEC 2003
L8          29456 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L9           8321 S L8 AND (GAG OR POL)
L10          3348 S L9 AND (GAG AND POL)
L11           430 S L10 AND (AVIPOX OR FOWLPOX OR FOWL POX)
L12           202 S L11 AND (FOWLPOX OR FOWL POX OF FPV)
L13            28 S L12 AND (GAG/CLM OR POL/CLM OR FOWLPOX/CLM OR FPV/CLM OR FOWL
L14           319 S L11 AND (CYTOKINE? OR INTERLEUKIN? OR INTERFERON?)
L15            32 S L14 AND (CYTOKINE?/CLM OR INTERLEUKIN?/CLM OR INTERFERON?/CLM
L16            28 S L15 NOT L13
L17           307 S (CYTOKINE? (5W) ADJUVANT?)
L18           272 S L17 AND VACCIN?
L19            89 S L18 AND (CYTOKINE?/CLM)
L20            55 S L19 AND (VIRUS/CLM OR VIRAL/CLM OR VACCINE/CLM)

     FILE 'MEDLINE' ENTERED AT 19:24:53 ON 09 DEC 2003
L1         136279 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L2           7106 S L1 AND (CYTOKINE? OR INTERLEUKIN? OR INTERFERON?)
L3            126 S L2 AND (ADJUVANT)
L4             46 S L3 AND PY<1999
L5          68868 S (INTERLEUKIN-2 OR IL-2 OR GAMMA INTERFERON OR INTERFERON GAMM
L6           3030 S L5 AND ADJUVANT?
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L7	1412	S	L6 AND ADJUVANT?/AB
L8	282	S	L7 AND ADJUVANT?/TI
L9	168	S	L8 AND (IL-2/AB OR INTERLEUKIN-2/AB)
L10	108	S	L9 AND PY<1999
		E	PAOLETTI ENZO/AU
		E	E1
L11	173	S	E2
L12	40	S	L11 AND (TROVAC OR ALVAC OR NYVAC)
L13	1	S	L12 AND ADJUVANT?
L14	25	S	CYTOKINE ADJUVANT?

L35 ANSWER 2 OF 3 USPATFULL on STN
1999:15497 Recombinant vaccine.
Ramshaw, Ian Allister, Australian Capital Territory, Australia
Boyle, David Bernard, Victoria, Australia
Coupar, Barbara Elizabeth Howieson, Victoria, Australia
Andrew, Marion Elizabeth, Victoria, Australia
Commonwealth Scientific and Industrial Organisation, Australian Capital Territory, Australia (non-U.S. corporation)The Australian National University, Australian Capital Territory, Australia (non-U.S. corporation)
US 5866136 19990202
APPLICATION: US 1990-611112 19901109 (7)
PRIORITY: AU 1986-7212 19860801
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A recombinant vaccine comprises a vaccine vector which incorporates a first nucleotide sequence capable of being expressed as all or a part of an antigenic polypeptide, together with a second nucleotide sequence capable of being expressed as all or a part of a lymphokine effective in enhancing the immune response to the antigenic polypeptide. The vaccine vectors include poxvirus, herpes virus or adenovirus, and the lymphokine may be an interleukin, tumour necrosis factor or gamma-interferon. The vaccine vector may express an antigenic polypeptide which is foreign to the host vector.

CLM What is claimed is:
1. A preparation for stimulating an immune response in a human or animal host comprising a vaccinia virus **vector** incorporating a **first nucleotide sequence** capable of being expressed as an **antigenic polypeptide** which is foreign to the host vector, together with a **second nucleotide sequence** capable of being expressed as a polypeptide having **lymphokine activity** selected from the group consisting of interleukin-2, interleukin-3, interleukin-4, interleukin-5, .gamma.-interferon and tumour necrosis factor, and which is effective in enhancing the immune response in the human or animal host to the antigenic polypeptide when compared to the immune response in the human or animal host administered a vaccinia virus vector incorporating only the first nucleotide sequence.

2. A method for the production of the preparation according to claim 1, which comprises the step of inserting into a vaccinia virus vector a nucleotide sequence capable of being expressed as a polypeptide having lymphokine activity selected from the group consisting of interleukin-2, interleukin-3, interleukin-4, interleukin-5, .gamma.-interferon and tumour necrosis factor, said method further comprising inserting into the vector a nucleotide sequence capable of being expressed as an antigenic polypeptide which is foreign to the host.

3. A method for producing an immune response in a human or animal which comprises the step of administering to the human or animal a preparation according to claim 1.

L35 ANSWER 3 OF 3 USPATFULL on STN
1999:15492 Recombinant vaccine.
Ramshaw, Ian Allister, Duffy, Australia
Boyle, David Bernard, Leopold, Australia
Coupar, Barbara Elizabeth Howieson, East Geelong, Australia
Andrew, Marion Elizabeth, Belmont, Australia
Commonwealth Scientific and Industrial Research Organisation, Australia

(non-U.S. government)The Australian National University, Australia
(non-U.S. corporation)
US 5866131 19990202
APPLICATION: US 1995-473301 19950607 (8)
PRIORITY: AU 1986-7212 19860801
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A recombinant vaccine comprises a vaccine vector which incorporates a first nucleotide sequence capable of being expressed as all or a part of an antigenic polypeptide, together with a second nucleotide sequence capable of being expressed as all or a part of a lymphokine effective in enhancing the immune response to the antigenic polypeptide. The vaccine vectors include poxvirus, herpes virus or adenovirus, and the lymphokine may be an interleukin, tumour necrosis factor or gamma-interferon. The vaccine vector may express an antigenic polypeptide which is foreign to the host vector.

CLM What is claimed is:

1. A preparation for stimulating an immune response to an antigenic polypeptide in a human or animal host, comprising a **vector** for expressing an antigenic polypeptide in said human or animal host, said vector incorporating a **first nucleotide sequence** which is expressed as said **antigenic polypeptide**, together with a **second nucleotide sequence** which is expressed as a polypeptide having **lymphokine activity** and which is effective in enhancing the immune response in said human or animal host to the antigenic polypeptide when compared to the immune response in said human or animal host administered a vector incorporating only the first nucleotide sequence, wherein said polypeptide having lymphokine activity is co-expressed with said antigenic polypeptide in said human or animal host.

2. A preparation according to claim 1, wherein the antigenic polypeptide is foreign to the vector.

3. A preparation according to claim 1, wherein the polypeptide having lymphokine activity is selected from the group consisting of interleukin-1, interleukin-2, interleukin-3, interleukin-4, interleukin-5, .gamma.-interferon and tumour necrosis factor.

4. A preparation according to claim 1, wherein the first nucleotide sequence is expressed as an antigenic polypeptide of the human immunodeficiency virus.

5. A preparation according to claim 1, wherein the first nucleotide sequence is expressed as an antigenic polypeptide of the influenza virus.

6. A preparation according to claim 1 wherein said vector is a virus.

7. A preparation according to claim 6, wherein the virus is selected from the group consisting of poxvirus, herpes virus and adenovirus.

8. A preparation according to claim 7, wherein said virus is a poxvirus.

9. A preparation according to claim 8, wherein said virus is vaccinia virus.

10. A method of stimulating an immune response to an antigenic polypeptide in a human or animal host, which comprises the step of

administering to the human or animal host a preparation according to claim 2.

11. A preparation according to claim 2, wherein the polypeptide having lymphokine activity is selected from the group consisting of interleukin-1, interleukin-2, interleukin-3, interleukin-4, interleukin-5, .gamma.-interferon and tumour necrosis factor.

12. A preparation according to claim 2, wherein the first nucleotide sequence is expressed as an antigenic polypeptide of the human immunodeficiency virus.

13. A preparation according to claim 2, wherein the first nucleotide sequence is expressed as an antigenic polypeptide of the influenza virus.

14. A preparation according to claim 2, wherein said vector is a virus.

15. A preparation according to claim 4, wherein the virus is selected from the group consisting of poxvirus, herpes virus and adenovirus.

16. A method for the production of the preparation according to claim 2, which comprises the step of inserting into said vector a first nucleotide sequence which is expressed as an antigenic polypeptide which is foreign to the vector, together with a second nucleotide sequence which is expressed as a polypeptide having lymphokine activity and which is effective in enhancing the immune response in said human or animal host to the antigenic polypeptide when compared to the immune response in said human or animal host administered a vector incorporating only the first nucleotide sequence wherein said polypeptide having lymphokine activity is co-expressed with said antigenic polypeptide in said human or animal host.

17. A method of stimulating an immune response to an antigenic polypeptide in a human or animal host, which comprises the step of administering to the human or animal host a preparation according to claim 1.

L37 ANSWER 2 OF 2 USPATFULL on STN
94:104326 Pox virus vaccine.
Boyle, David B., Leopold, Australia
Kumar, Sharad, Herne Hill, Australia
Commonwealth Science and Industrial Research Organisation, Campbell, Australia (non-U.S. corporation)
US 5368855 19941129
APPLICATION: US 1992-993073 19921218 (7)
PRIORITY: AU 1988-6721 19880212
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A gene sequence including a first promoter for the expression of a major early fowlpox virus (FPV) protein. In a preferred aspect, the gene sequence further includes a second promoter for the expression of a late fowlpox virus protein in opposite orientation to said first promoter. The promoter is useful in developing FPV based vectors for the delivery of vaccine antigens preferably to poultry, and as a tool to study the temporal regulation of poxvirus genes. The invention also offers methods useful in the construction of recombinant fowlpox viruses or related avian poxviruses, which methods are characterized by the introduction of foreign DNA into the fowlpox virus or into virus DNA sequences, which sequences are able to use native FPV promoter regions.

CLM What is claimed is:

1. A vaccine including a viral vector, said viral vector including: a portion of the genome of a vector virus; a bidirectional promoter element including a first promoter which controls expression of an early viral protein in fowlpox virus and a second promoter which controls expression of a late viral protein in fowlpox virus, said second promoter being in an opposite orientation to said first promoter, wherein said bidirectional promoter element has the sequence
5'AGCCATTTAGTATCCTAAAATTGAATTGTAATTATCGATAATAAATGCAC 3' (SEQ ID NO: 10)
3'TCGGTAAATCATAGGATTTTAACTTAACATTAATAGCTATTATTTACCTG 5' (SEQ ID NO: 11)
and a first foreign DNA sequence coding for a first foreign gene of interest and under the control of said first promoter; or a second foreign DNA sequence coding for a second foreign gene of interest and under the control of said second promoter; or a first foreign DNA sequence coding for a first foreign gene of interest and under the control of said first promoter together with a second foreign DNA sequence coding for a second foreign gene of interest and under the control of said second promoter.

2. A vaccine including a viral vector according to claim 1, wherein the portion of the genome of a virus is a portion of the fowlpox virus genome or vaccinia virus genome.

3. A vaccine including a viral vector according to claim 1, wherein the first foreign DNA sequence codes for a first antigen characteristic of an avian disease.

4. A vaccine including a viral vector according to claim 1, wherein the second foreign DNA sequence codes for a second antigen characteristic of an avian disease.

L13 ANSWER 21 OF 28 USPATFULL on STN
2000:105429 Methods for generating immune responses employing modified vaccinia of fowlpox viruses.
Dorner, Friedrich, Vienna, Austria
Scheiflinger, Friedrich, Orth/Donau, Austria
Falkner, Falko Gunter, Mannsdorf, Austria
Pfleiderer, Michael, Breitstetten, Austria
Immuno AG., Vienna, Austria (non-U.S. corporation)
US 6103244 20000815
APPLICATION: US 1996-651472 19960522 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is disclosed for producing a modified eukaryotic cytoplasmic DNA virus by direct molecular cloning of a modified DNA molecule comprising a modified cytoplasmic DNA virus genome. The inventive method comprises the steps of (I) modifying under extracellular conditions a DNA molecule comprising a first cytoplasmic DNA virus genome to produce a modified DNA molecule comprising the modified cytoplasmic DNA virus genome; (II) introducing the modified DNA molecule into a first host cell which packages the modified DNA molecule into infectious virions; and (III) recovering from the host cell virions comprised of the modified viral genome. The host cell is infected with a helper virus which is expressed to package the modified viral genome into infectious virions. Examples of packaging a modified poxvirus genome by a helper poxvirus of the same or different genus are described. Also disclosed are novel poxvirus vectors for direct molecular cloning of open reading frames into a restriction enzyme cleavage site that is unique in the vector. In one model poxvirus vector, the open reading frame is transcribed by a promoter located in the vector DNA upstream of a

multiple cloning site comprised of several unique cleavage sites.

CLM What is claimed is:

1. A method for generating an immune response in a vertebrate against a heterologous protein comprising the following steps: (a) providing a modified vaccinia virus containing a heterologous insert encoding an immunogenic protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site; (b) administering the modified vaccinia virus to the vertebrate in an amount sufficient to generate the immune response.

2. The method according to claim 1, wherein the protein is a viral protein.

3. The method according to claim 2, wherein the protein is selected from the group consisting of HIV gp160, HIV Gag
, and HIV Gag-Pol.

4. The method according to claim 1, wherein the cleavage site is recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII.

5. A method for priming an immune response in a vertebrate comprising the following steps: (a) providing a modified vaccinia virus containing a heterologous insert encoding an immunogenic protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site; (b) administering the modified vaccinia virus to the vertebrate in an amount sufficient to prime the immune response.

6. The method according to claim 5, wherein the protein is a viral protein.

7. The method according to claim 6, wherein the protein is selected from the group consisting of HIV gp160, HIV Gag
, and HIV Gag-Pol.

8. The method according to claim 5, wherein the cleavage site is recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII.

9. A method for generating an immune response in a vertebrate against a heterologous protein comprising the following steps: (a) providing a modified fowlpox virus containing a heterologous insert encoding an immunogenic protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII; (b) administering the modified fowlpox virus to the vertebrate in an amount sufficient to generate the immune response.

10. The method according to claim 9, wherein the protein is a viral protein.

11. The method according to claim 10, wherein the protein is selected from the group consisting of HIV gp160, HIV
Gag, and HIV Gag-Pol.

12. A method for priming an immune response in a vertebrate against a heterologous protein comprising the following steps: (a) providing a modified fowlpox virus containing a heterologous insert

encoding an immunogenic protein, wherein said insert was molecularly cloned directly into the viral genome into a unique restriction endonuclease cleavage site recognized by a restriction endonuclease selected from the group consisting of NotI, SmaI, ApaI, and RsrII; (b) administering the modified fowlpox virus to the vertebrate in an amount sufficient to prime the immune response.

13. The method according to claim 12, wherein the protein is a viral protein.

14. The method according to claim 13, wherein the protein is selected from the group consisting of HIV gp160, HIV Gag, and HIV Gag-Pol.

L13 ANSWER 22 OF 28 USPATFULL on STN
1999:12561 Recombinant attenuated ALVAC canaryopox virus containing heterologous HIV or SIV inserts.
Paoletti, Enzo, Delmar, NY, United States
Tartaglia, James, Schenectady, NY, United States
Cox, William I., Troy, NY, United States
Virogenetics Corporation, Troy, NY, United States (U.S. corporation)
US 5863542 19990126
APPLICATION: US 1995-417210 19950405 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Attenuated recombinant viruses containing DNA encoding an immunodeficiency virus and/or CTL antigen, as well as methods and compositions employing the viruses, expression products therefrom, and antibodies generated from the viruses or expression products, are disclosed and claimed. The recombinant viruses can be NYVAC or ALVAC recombinant viruses. The DNA can code for at least one of: HIV1gag(+pro)(IIIB), gp120(MN)(+transmembrane), nef(BRU)CTL, pol (IIIB)CTL, ELDKWA or LDKW epitopes, preferably HIV1gag(+pro)(IIIB), gp120(MN) (+transmembrane), two (2) nef(BRU)CTL and three (3) pol(IIIB)CTL epitopes; or two ELDKWA in gp120 V3 or another region or in gp160. The two (2) nef(BRU)CTL and three (3) pol (IIIB)CTL epitopes are preferably CTL1, CTL2, pol1, pol2 and pol3. The recombinant viruses and gene products therefrom and antibodies generated by the viruses and gene products have several preventive, therapeutic and diagnostic uses. DNA from the recombinant viruses are useful as probes or, for generating PCR primers or for immunization. Also disclosed and claimed are HIV immunogens and modified gp160 and gp120.

CLM What is claimed is:
1. A recombinant attenuated canarypox virus comprising an ALVAC canarypox virus and an exogenous DNA segment encoding a human or simian immunodeficiency virus gene product.

2. The recombinant virus of claim 1 wherein the exogenous DNA encodes HIV1gag(+pro)(IIIB), gp120 (MN) (+transmembrane) and two nef(BRU)CTL epitopes.

3. The virus of claim 2 wherein the two nef(BRU)CTL epitopes are CTL1 and CTL2.

4. The virus of claim 2 which is vCP264.

5. The virus of claim 1 wherein the exogenous DNA encodes gp120

(MN)(+transmembrane) and two ELDKWA (SEQ ID NO: 147) epitopes in the gp120 V3 loop region.

6. The virus of claim 5 which is vCP1307.

7. The virus of claim 1 wherein the exogenous DNA encodes HIV1gag(+pro)(IIIB) and gp120(MN)(+transmembrane).

8. The virus of claim 7 which is vCP205.

9. The virus of claim 1 wherein the exogenous DNA encodes HIV1gag(+pro)(IIIB), gp120(MN) (+transmembrane) and two nef(BRU) and three pol(IIIB) CTL epitope containing regions.

10. The virus of claim 9 wherein the two nef(BRU)CTL and three pol(IIIB)CTL epitopes are: CTL1, CTL2, pol1, pol2 and pol3.

11. The virus of claim 9 which is vCP300.

12. A immunogenic composition comprising a recombinant virus as claimed in any one of claims 1 to 11 and a carrier.

13. A method for expressing a human or simian immunodeficiency gene product comprising infecting a suitable host cell with a recombinant virus as claimed in any one of claims 1 to 11.

14. A method for inducing an immunogical response to a human or simian immunodeficiency gene product comprising administering a recombinant virus as claimed in any one of claims 1 to 11.

15. A method for inducing an immunogical response to a human or simian immunodeficiency gene product comprising administering a composition as claimed in claim 12.

16. The method of claim 14 further comprising subsequently administering an antigen derived from human or simian immunodeficiency, whereby the administation of the recombinant virus is a priming administration and the administration of the antigen derived from human or simian immunodeficiency virus is a booster administration.

17. The method of claim 15 further comprising subsequently administering an antigen derived from human or simian immunodeficiency, whereby the administration of the composition is a priming administration and the administration of the antigen derived from human or simian immunodeficiency virus is a booster administration.

L13 ANSWER 24 OF 28 USPATFULL on STN
1998:68530 Trova fowl pox virus recombinants comprising heterologous inserts.
Paoletti, Enzo, Delmar, NY, United States
Perkus, Marion E., Altamont, NY, United States
Taylor, Jill, Albany, NY, United States
Tartaglia, James, Schenectady, NY, United States
Norton, Elizabeth K., Latham, NY, United States
Riviere, Michel, Ecully, France
de Taisne, Charles, Lyons, France
Limbach, Keith J., Troy, NY, United States
Johnson, Gerard P., Waterford, NY, United States
Pincus, Steven E., East Greenbush, NY, United States
Cox, William I., Troy, NY, United States

Audonnet, Jean-Christophe Francis, Albany, NY, United States
Gettig, Russell Robert, Averill Park, NY, United States
Virogenetics Corporation, Troy, NY, United States (U.S. corporation)
US 5766599 19980616
APPLICATION: US 1995-458101 19950601 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB What is described is a modified vector, such as a recombinant poxvirus, particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open reading frame encoding a virulence factor. In another embodiment, the genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant virus vaccines.

CLM What is claimed is:
1. An attenuated virus having all the identifying characteristics of: a **TROVAC fowlpox virus**.

2. A virus which is TROVAC.

3. A vector which comprises the virus of claim 1.

4. A vector which comprises the virus of claim 2.

5. A virus as claimed in claim 2 further comprising exogenous DNA from a non-poxvirus source in a nonessential region of the virus genome.

6. A virus as claimed in claim 5 wherein the exogenous DNA is selected from the group consisting of rabies virus, Hepatitis B virus, Japanese encephalitis virus, yellow fever virus, Dengue virus, measles virus, pseudorabies virus, Epstein-Barr virus, herpes simplex virus, **human immunodeficiency virus**, simian immunodeficiency virus, equine herpes virus, bovine herpes virus, bovine viral diarrhea virus, human cytomegalovirus, canine parvovirus, equine influenza virus, feline leukemia virus, feline herpes virus, Hantaan virus, C. tetani, avian influenza virus, mumps virus and Newcastle Disease virus.

7. A virus as claimed in claim 6 wherein the non-poxvirus source is avian influenza virus and the fowlpox virus is vFP89, vFP92, vFP100 or vFP122.

8. A virus as claimed in claim 6 wherein the virus is a fowlpox virus, the non-poxvirus source is human immunodeficiency virus and the fowlpox virus is vFP62, vFP63 or vFP174.

9. A virus as claimed in claim 6 wherein the non-poxvirus source is Newcastle Disease virus and the fowlpox virus is vFP96.

10. A virus as claimed in claim 6 which is a human immunodeficiency virus recombinant fowlpox virus which is vFP62 or vFP63.

11. A virus as claimed in claim 1 further comprising exogenous DNA from a non-poxvirus source in a nonessential region of the virus genome.

12. An immunological composition for inducing an immunological response in a host animal inoculated with said composition, said composition comprising the virus of any one of claims 1, 2 or 10 or 11, or, a vector as claimed in claim 3 or 4, and a carrier.

13. The immunological composition of claim 12 containing the virus or vector in an amount sufficient to induce a protective immunological response such that the immunological composition is a vaccine.

14. A method of expressing a gene product in a cell cultured in vitro comprising introducing into the cell a virus as claimed in any one of claims 1, 2 or 10 or 11, or, a vector as claimed in claim 3 or 4, transforming cell with the expression vector, cultivating the transformed cell under conditions which allow expression of the gene product, and further purifying the product.

L13 ANSWER 25 OF 28 USPATFULL on STN
1998:68529 Recombinant attenuated ALVAC canarypoxvirus expression vectors containing heterologous DNA segments encoding lentiviral gene products.
Paoletti, Enzo, Delmar, NY, United States
Tartaglia, James, Schenectady, NY, United States
Cox, William Irvin, Troy, NY, United States
Virogenetics Corporation, Troy, NY, United States (U.S. corporation)
US 5766598 19980616
APPLICATION: US 1994-303275 19940907 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention is directed toward recombinant attenuated canarypox virus expression vectors containing exogenous DNA segments encoding lentiviral gene products. A parental canarypox virus (Rentschler strain) was obtained and attenuated through more than 200 serial passages on chick embryo fibroblasts. A master viral seed was subjected to four successive plaque purifications under agar and one plaque clone was amplified through five additional passages after which the stock virus was used as the parental virus in in vitro recombination studies. This attenuated plaque purified canarypox isolate was designated ALVAC. A series of ALVAC recombinants were generated that are capable of expressing different HIV and SIV gene products including Gag, Pol, Env, and Nef. These recombinants provide useful reagents for the generation of viral-specific immune responses.

CLM What is claimed is:
1. A **recombinant attenuated ALVAC canarypox virus** comprising an exogenous DNA segment encoding a lentivirus gene product.

2. The recombinant virus of claim 1 wherein the exogenous DNA segment encodes a human immunodeficiency virus or simian immunodeficiency virus gene product.

3. The recombinant virus of claim 2 wherein the exogenous DNA segment encodes a human immunodeficiency virus gene product.

4. The recombinant virus of claim 2 wherein the exogenous DNA segment encodes a simian immunodeficiency virus gene product.

5. The recombinant virus of claim 1 wherein said exogenous DNA segment further encodes a human T-helper lymphocyte epitope derived from tetanus toxoid fragment C.

6. The recombinant virus of claim 5 wherein said exogenous DNA segment encodes a human immunodeficiency virus or simian immunodeficiency virus gene product.

7. The recombinant virus of claim 6 wherein said exogenous DNA segment encodes a human immunodeficiency virus gene product.

8. The recombinant virus of claim 6 wherein said exogenous DNA segment encodes a simian immunodeficiency virus gene product.

9. A recombinant attenuated ALVAC canarypox virus selected from the group consisting of vCP95, vCP112, vCP60, vCP61, vCP125, vCP124, vCP126, vCP144, vCP120, vCP138, vCP117, vCP130, vCP152, vCP155, vCP156, vCP146, vCP148, vCP154, vCP168, vCP153, and vCP172.

10. The **recombinant virus** of claim 1 wherein the gene product is selected from the group consisting of: gp160; gp120; **Gag and Pol**; Gag, Pol and gp120; Gag, Pol and gp160; Gag, Pol and truncated Env; non-cleavable gp160; gp120 anchored with transmembrane; Gag, Pol, and gp120 anchored with transmembrane; signal domain of Env and p24 fused to T1 and V3 loop of Env; p24 fused to T1 and V3 loop of Env; Nef; V3 loop fused to 88 epitope; T1, T2, and TH4.1 epitopes; Env signal domain, T1, T2, and TH4.1 epitopes; and; Gag, Pol protease and gp120 anchored with a transmembrane sequence.

11. An immunogenic composition comprising a recombinant attenuated canarypox virus as claimed in any one of claims 1 to 10 and an adjuvant.

12. A method for expressing a lentiviral gene product comprising infecting a suitable host cell with a recombinant attenuated canarypox virus as claimed in any one of claims 1 to 10.

13. A method of inducing an immunological response to a lentivirus gene product comprising administering a recombinant attenuated canarypox virus as claimed in any one of claims 1 to 10.

14. A method of inducing an immunological response to a lentivirus gene product comprising administering an immunogenic composition as claimed in claim 11.

L13 ANSWER 26 OF 28 USPATFULL on STN
97:86478 Recombinant fowlpox virus.
Dorner, Friedrich, Vienna, Austria
Scheiflinger, Friedrich, Orth/Donau, Austria
Falkner, Falko Gunter, Mannsdorf, Austria
Immuno Aktiengesellschaft, Vienna, Austria (non-U.S. corporation)
US 5670367 19970923
APPLICATION: US 1994-232463 19940422 (8)
PRIORITY: EP 1991-114300 19910826
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An improved method is described to prepare recombinant fowlpox

virus for the expression of proteins or for use as a vaccine. The new method uses for the insertion of foreign DNA an intergenic region which is located between the FPV thymidine kinase (tk)gene and the 3'-open reading frame. Said intergenic region is enlarged to comprise one or more unique restriction sites, thereby allowing insertion of foreign DNA in such a way that the FPV tk-gene remains intact and codes for the entire thymidine kinase. New strong poxvirus promoters are presented and new FPV host virus strains carrying a vaccinia virus thymidine kinase gene and an E. coli lacZ gene as a novel non-essential site. The novel fowlpox virus host strains allow the use of any insertion plasmid carrying vaccinia virus tk-gene flanking regions.

CLM What is claimed is:

1. **Recombinant fowlpox virus**, wherein the 3'-region downstream of the fowlpox virus P2 gene is used as a non-essential site for the insertion of foreign DNA.

2. A recombinant fowlpox virus having a thymidine kinase gene and an adjacent, downstream open reading frame separated from said thymidine kinase gene by an intergenic region, wherein said recombinant fowlpox virus has inserted into said intergenic region a foreign DNA sequence and a poxvirus promoter to cause expression of said foreign DNA sequence, wherein said poxvirus promoter is a fowlpox P2 promoter.

3. A plasmid comprising the fowlpox P2 promoter.

4. A plasmid comprising the FPV P2 promoter, the P2 gene and the 3'-sequence as shown in SEQ ID NO:19 or a functional equivalent thereof.

5. A plasmid comprising a fowlpox thymidine kinase gene, a downstream intergenic region adjacent to said thymidine kinase gene and a downstream fowlpox open reading frame adjacent to said downstream intergenic region, such that said downstream intergenic region is located between said thymidine kinase gene and said downstream fowlpox open reading frame, wherein said intergenic region comprises at least one site for insertion of foreign DNA into said intergenic region, wherein said plasmid further comprises: (a) a fowlpox P2 promoter linked to a foreign DNA sequence to be expressed; (b) a poxvirus promoter linked to a gene encoding a marker or indicator for selection of recombinant fowlpox virus, wherein element (a) and element (b) form a construct; and (c) DNA sequences of fowlpox virus flanking said construct of elements (a) and (b), wherein said flanking sequences have homology with sequences upstream and downstream of the intergenic region or within the intergenic region to permit insertion of said construct into fowlpox.

6. Plasmid pTZgpt-P2a of FIG. 9.

7. Plasmid pTZgpt-P2b of FIG. 9.

8. Isolated fowlpox promoter P2.

9. An isolated fowlpox promoter according to claim 8, wherein said promoter comprises a sequence set forth at bases 1-174 of SEQ ID NO:19.

L15 ANSWER 32 OF 35 USPATFULL on STN
2001:109978 METHOD OF DNA VACCINATION.
OLSEN, CHRISTOPHER W., MADISON, WI, United States

SWAIN, WILLIAM F., MADISON, WI, United States
LARSEN, DIANE L., SUN PRARIE, WI, United States
NEUMANN, VERONICA C., MIDDLETON, WI, United States
LUNN, DAVID P., BROOKLYN, WI, United States
US 2001007860 A1 20010712
APPLICATION: US 1998-113836 A1 19980710 (9)
PRIORITY: US 1997-52441P 19970714 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of providing a patient with an enhanced immune response is disclosed. In one embodiment, the method comprises the step of vaccinating the patient with a vaccine comprising a combination of DNA encoding interleukin-6 and DNA encoding an antigen capable of enlisting an enhanced immune response in a patient. In one embodiment, the enhanced immune response is a therapeutic response. In another embodiment, the enhanced immune response is a protective immune response.

CLM What is claimed is:

1. A method for eliciting an **enhanced immune response** against a selected antigen in a mammalian subject, said method comprising administering to said subject a composition comprising a **first nucleic acid sequence encoding interleukin-6** and a **second nucleic acid sequence encoding the selected antigen**, wherein said first and second nucleic acid sequences are operably linked to control sequences which direct the expression thereof in said subject.

2. The method of claim 1, wherein the first and second sequences are present in a single nucleic acid construct.

3. The method of claim 1, wherein the enhanced immune response is characterized by the generation of an enhanced antibody response against said antigen.

4. The method of claim 1, wherein the enhanced immune response is characterized by the generation of an enhanced T-cell response against said antigen.

5. The method of claim 1, wherein the composition is a therapeutic vaccine composition.

6. The method of claim 1, wherein the composition is a prophylatic vaccine composition.

7. The method of claim 3, wherein the antibody response is protective.

8. The method of claim 1, wherein the selected antigen is a viral antigen.

9. The method of claim 1, wherein the selected antigen is a bacterial antigen.

10. The method of claim 1, wherein the selected antigen is a tumor antigen.

11. The method of claim 1, wherein the composition is administered using particle-mediated delivery techniques.

12. The method of claim 1, wherein the composition is administered to a

target skin site in said subject.

13. The method of claim 1, wherein the composition is administered to a target mucosal surface in said subject.

14. The method of claim 13, wherein the composition is administered to the tongue.

15. The method of claim 1, wherein the viral antigen is derived from a virus selected from the group consisting of influenza viruses, rotaviruses, herepes viruses, and hepatitis viruses.

16. The method of claim 15, wherein the virus is an influenza virus.

17. The method of claim 15, wherein the virus is a hepatitis virus.

L38 ANSWER 3 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-376522 [32] WPIDS
DNC C2000-113924
TI A novel fowl pox virus vector coding a HIV antigen and a cytokine, useful for inducing an immune response to a HIV- 1 antigen.
DC B04 C06 D16
IN BOYLE, D B; KENT, S; RAMSHAW, I A
PA (BOYL-I) BOYLE D B; (CSIR) COMMONWEALTH SCI & IND RES ORG; (MACF-N) MACFARLANE BURNET CENT MEDICAL; (AUSU) UNIV AUSTRALIAN NAT; (VIRA-N) VIRAX HOLDINGS LTD; (VIRA-N) VIRAX IMMUNOTHERAPEUTICS PTY LTD
CYC 91

PI WO 2000028003 A1 20000518 (200032)* EN 48p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000015014 A 20000529 (200041)
EP 1129177 A1 20010905 (200151) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002529076 W 20020910 (200274) 47p
NZ 511567 A 20030926 (200366)
ADT WO 2000028003 A1 WO 1999-AU989 19991109; AU 2000015014 A AU 2000-15014 19991109; EP 1129177 A1 EP 1999-957232 19991109, WO 1999-AU989 19991109; JP 2002529076 W WO 1999-AU989 19991109, JP 2000-581170 19991109; NZ 511567 A NZ 1999-511567 19991109, WO 1999-AU989 19991109
FDT AU 2000015014 A Based on WO 2000028003; EP 1129177 A1 Based on WO 2000028003; JP 2002529076 W Based on WO 2000028003; NZ 511567 A Div in NZ 527045, Based on WO 2000028003
PRAI AU 1998-7007 19981109

AB WO 200028003 A UPAB: 20000706
NOVELTY - A novel avipox virus vector encoding a HIV antigen and a cytokine to enhance the immune response.

DETAILED DESCRIPTION - A novel recombinant viral construct (I) comprises an avipox viral vector comprising a first nucleic acid (NA) encoding one or more HIV antigens, and a second NA encoding a cytokine, wherein (I) is effective in stimulating an immune response to the HIV antigen.

INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine composition comprising (I);

(2) a pharmaceutical composition comprising (I);

(3) stimulating an immune response to HIV, comprising administering to the mammal (I) or (1); and

(4) the treatment and/or prophylaxis of HIV infection or AIDS in a mammal comprising administering (I) or (1) to stimulate an immune response to one or more HIV antigen.

USE - The viral constructs and methods are used for the treatment and prophylaxis of HIV infection, especially HIV-1 infection. The vectors are used to induce an immune response against HIV. There are also used in the manufacture of pharmaceutical compositions for the treatment or prophylaxis of HIV infections (claimed).

ADVANTAGE - Prior art avipox HIV vaccines induce a response that is often weak, transient, or non-existent. The present invention provides avipox vaccines which over come these problem, by also expressing a cytokine, which results in an enhanced immune response.

DESCRIPTION OF DRAWING(S) - The figure is a schematic representation

of the construction of FPVgag/pol-IFN gamma .
Dwg.1/6

L38 ANSWER 7 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1988-049975 [07] WPIDS
DNC C1988-022180
TI New recombinant vaccine contg. sequences expressing antigen - in viral vector, useful in immuno-deficient subjects, esp. patients infected with HIV.
DC B04 D16
IN ANDREW, M E; BOYLE, D B; COUPAR, B E; RAMSHAW, I A; ANDREW, M; COUPAR, B E H; RAMSHAW, I
PA (CSIR) COMMONWEALTH SCI & IND RES ORG; (RAMS-I) RAMSHAW I A; (AUSU) UNIV AUSTRALIAN NAT
CYC 17

PI WO 8800971 A 19880211 (198807)* EN 32p
RW: AT BE CH DE FR GB IT LU NL SE
W: AU JP KR US
AU 8777899 A 19880224 (198820)
ZA 8705681 A 19880219 (198821)
EP 275300 A 19880727 (198830) EN
R: AT BE CH DE FR GB IT LI LU NL SE
JP 01500755 W 19890316 (198917)
EP 275300 A4 19890118 (199327)
EP 275300 B1 19960103 (199606) EN 22p
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3751664 G 19960215 (199612)
JP 2642113 B2 19970820 (199738) 15p
CA 1339346 C 19970826 (199748)
US 5866131 A 19990202 (199912)
US 5866136 A 19990202 (199912)
KR 9708217 B1 19970522 (199942)

ADT WO 8800971 A WO 1987-AU246 19870731; ZA 8705681 A ZA 1987-5681 19870731; EP 275300 A EP 1987-905142 19870731; JP 01500755 W JP 1987-504750 19870731; EP 275300 A4 EP 1987-905142 19870731, WO 1987-AU246 19870731; EP 275300 B1 EP 1987-905142 19870731, WO 1987-AU246 19870731; DE 3751664 G DE 1987-3751664 19870731, EP 1987-905142 19870731, WO 1987-AU246 19870731; JP 2642113 B2 JP 1987-504750 19870731, WO 1987-AU246 19870731; CA 1339346 C CA 1987-543498 19870731; US 5866131 A Cont of WO 1987-AU246 19870731, Cont of US 1988-203060 19880601, CIP of US 1990-498420 19900326, Cont of US 1990-611112 19901109, US 1995-473301 19950607; US 5866136 A Cont of WO 1987-AU246 19870731, Cont of US 1988-203060 19880601, CIP of US 1990-498420 19900326, US 1990-611112 19901109; KR 9708217 B1 WO 1987-AU246 19870731, KR 1988-700347 19880401

FDT EP 275300 A4 Based on WO 8800971; EP 275300 B1 Based on WO 8800971; DE 3751664 G Based on EP 275300, Based on WO 8800971; JP 2642113 B2 Previous Publ. JP 01500755, Based on WO 8800971

PRAI AU 1986-7212 19860801; AU 1987-77899 19860725

AB **WO 8800971 A UPAB: 19930923**
Recombinant vaccine comprises a vaccine vector which includes (1) a nucleotide sequence (NS1) expressing at least part of an antigenic polypeptide (I) and (2) a second sequence (NS2) expressing at least part of a lymphokine (II) which increases immune response to (I).

The vector is a pox, herpes or adeno virus, most esp. vaccinia, and (II) is interleukin 1,2,3 or 4, or gamma interferon.

USE/ADVANTAGE - The vaccine is useful in immunodeficient/immunosuppressed humans and animals, esp. patients infected with human immunodeficiency virus (HIV). The presence of (II) improves and/or modifies the response to co-expressed antigen, and

co-expression ensures that both components are produced by the same infected cells in a very localised area. Side-effects (generalised vaccinia infection) caused by using virus-based vaccines in immunodeficient patients are avoided.
0/8

L42 ANSWER 2 OF 4 MEDLINE on STN
1999030931 Document Number: 99030931. PubMed ID: 9811759. Enhanced T-cell immunogenicity and protective efficacy of a human immunodeficiency virus type 1 vaccine regimen consisting of consecutive priming with DNA and boosting with recombinant fowlpox virus. Kent S J; Zhao A; Best S J; Chandler J D; Boyle D B; Ramshaw I A. (AIDS Pathogenesis Research Unit, Macfarlane Burnet Centre for Medical Research, Fairfield 3078, Victoria, Australia.. kent@burnet.edu.au) . JOURNAL OF VIROLOGY, (1998 Dec) 72 (12) 10180-8. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The induction of human immunodeficiency virus (HIV)-specific T-cell responses is widely seen as critical to the development of effective immunity to HIV type 1 (HIV -1). Plasmid DNA and recombinant fowlpox virus (rFPV) vaccines are among the most promising safe HIV-1 vaccine candidates. However, the immunity induced by either vaccine alone may be insufficient to provide durable protection against HIV-1 infection. We evaluated a consecutive immunization strategy involving priming with DNA and boosting with rFPV vaccines encoding common HIV-1 antigens. In mice, this approach induced greater HIV-1-specific immunity than either vector alone and protected mice from challenge with a recombinant vaccinia virus expressing HIV-1 antigens. In macaques, a dramatic boosting effect on DNA vaccine-primed HIV-1-specific helper and cytotoxic T-lymphocyte responses, but a decline in HIV -1 antibody titers, was observed following rFPV immunization. The vaccine regimen protected macaques from an intravenous HIV-1 challenge, with the resistance most likely mediated by T-cell responses. These studies suggest a safe strategy for the enhanced generation of T-cell-mediated protective immunity to HIV-1.

L42 ANSWER 3 OF 4 MEDLINE on STN
97461115 Document Number: 97461115. PubMed ID: 9315482. DNA vaccination against virus infection and enhancement of antiviral immunity following consecutive immunization with DNA and viral vectors. Ramsay A J; Leong K H; Ramshaw I A. (Division of Immunology and Cell Biology, John Curtin School of Medical Research, Australian National University, Canberra, Australia.. Alistair.Ramsay@anu.edu.au) . IMMUNOLOGY AND CELL BIOLOGY, (1997 Aug) 75 (4) 382-8. Ref: 55. Journal code: 8706300. ISSN: 0818-9641. Pub. country: Australia. Language: English.

AB Recent demonstrations of the immunogenicity of antigens encoded in DNA plasmids following delivery by various routes have heralded a new era in vaccine development. In this article, we review progress in DNA-based antiviral immunoprophylaxis. Preclinical studies have already established the immunogenicity of DNA plasmids encoding protective antigens from a wide variety of viral pathogens and work published in recent months has raised real prospects of broadly protective DNA vaccination against infections with influenza virus and HIV. We also describe a consecutive immunization protocol consisting of a priming dose of vaccine antigen encoded in DNA plasmids followed by a booster with the same antigen encoded in recombinant fowlpox virus vectors. We have used this strategy to generate protective antiviral cell-mediated immunity and sustained, high-level antibody responses both systemically and at mucosae, and to elucidate immunological mechanisms underlying the development of immunity to antigens delivered in DNA vectors.

L42 ANSWER 4 OF 4 MEDLINE on STN
88014209 Document Number: 88014209. PubMed ID: 3498904. Recovery of

immunodeficient mice from a vaccinia virus/IL-2 recombinant infection. Ramshaw I A; Andrew M E; Phillips S M; Boyle D B; Coupar B E. (Department of Experimental Pathology, John Curtin School of Medical Research, Australian National University, Canberra.) NATURE, (1987 Oct 8-14) 329 (6139) 545-6. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Vaccinia virus recombinants that express cloned genes encoding antigens of unrelated infectious agents, such as hepatitis B virus and human immunodeficiency virus (HIV), provide a new approach to the development of live vaccines. Although there is evidence that genetically engineered vaccinia viruses have reduced pathogenicity a major obstacle to their use as vaccines is that severe complications can occur after vaccination, especially in immunodeficient individuals. We describe here a recombinant vaccinia virus expressing murine interleukin-2 (IL-2) and show that athymic nude mice infected with the recombinant virus resolve the virus infection rapidly whereas mice infected with control virus develop a progressive vaccinal disease. By incorporating the gene for IL-2 in live virus vaccines it may be possible to prevent the severe complications that arise in recipients with an impaired immune system.

L7 ANSWER 16 OF 29 MEDLINE on STN
95056040 Document Number: 95056040. PubMed ID: 7966603. Selective induction of immune responses by cytokines coexpressed in recombinant fowlpox virus. Leong K H; Ramsay A J; Boyle D B; Ramshaw I A. (Viral Engineering and Cytokine Research Group, John Curtin School of Medical Research, Australian National University, Canberra.) JOURNAL OF VIROLOGY, (1994 Dec) 68 (12) 8125-30. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Avipoxviruses have recently been studied as potential vectors for the delivery of heterologous vaccine antigen. **Because these viruses abortively infect mammalian cells yet still effectively present encoded foreign genes to the host immune system, they offer a safer but effective alternative to other live virus vectors. We have examined the effect of coexpressing the cytokine interleukin-6 or gamma interferon on immune responses to a recombinant fowlpox virus expressing influenza virus hemagglutinin.** The encoded cytokine was expressed for prolonged periods in infected cell culture with little cytopathic effect due to the abortive nature of the infection. In mice, vector-expressed cytokine dramatically altered immune responses induced by the coexpressed hemagglutinin antigen. **Expression of interleukin-6 augmented both primary systemic and mucosal antibody responses and primed for enhanced recall responses.** In contrast, expression of gamma interferon markedly inhibited antibody responses without affecting the generation of cell-mediated immunity. The safety of these constructs was demonstrated in mice with severe combined immunodeficiency, and no side effects due to cytokine expression were observed. **In summary, fowlpox virus vectors encoding cytokines represent a safe and effective vaccine strategy which may be used to selectively manipulate the immune response.**

L7 ANSWER 2 OF 29 MEDLINE on STN
1998078467 Document Number: 98078467. PubMed ID: 9416507. Cytokines and immunity to viral infections. Ramshaw I A; Ramsay A J; Karupiah G; Rolph M S; Mahalingam S; Ruby J C. (Division of Immunology and Cell Biology, John Curtin School of Medical Research, Australian National University, Canberra, Australia.) IMMUNOLOGICAL REVIEWS, (1997 Oct) 159 119-35. Ref: 96. Journal code: 7702118. ISSN: 0105-2896. Pub. country: Denmark. Language: English.

AB In this review, we discuss two broad approaches we have taken to study the role of cytokines and chemokines in antiviral immunity. Firstly, recombinant vaccinia viruses were engineered to express genes encoding cytokines and chemokines of interest. Potent antiviral activity was mediated by many of these encoded factors, including IL-2, IL-12, IFN-gamma, TNF-alpha, CD40L, Mig and Crg-2. In some cases, host defense mechanisms were induced (IL-2, IL-12, Mig and Crg-2), whilst for others, a direct antiviral effect was demonstrated (IFN-gamma, TNF-alpha and CD40L). In sharp contrast, vector-directed expression of IL-4, a type 2 factor, greatly increased virus virulence, due to a downregulation of host type 1 immune responses. Our second experimental approach involved the use of strains of mice deficient for the production of particular cytokines or their receptors, often in combination with our engineered viruses. Mice deficient in either IFN-gamma, IFN-gamma R, IFN-alpha/beta R, TNFRs, CD40 or IL-6 were, in general, highly susceptible to poxvirus infection. Surprisingly, not only the TNFR1, but also the TNFR2, was able to mediate the antiviral effects of TNF-alpha in vivo, whilst the antiviral activity observed following CD40-CD40L interaction is a newly defined function which may involve apoptosis of infected cells. Through the use of perforin-deficient mice, we were able to demonstrate a requirement for this molecule in the clearance of some viruses, such as ectromelia virus, whilst for others, such as vaccinia virus, perforin was less important but IFN-gamma was essential.

L7 ANSWER 3 OF 29 MEDLINE on STN
97461115 Document Number: 97461115. PubMed ID: 9315482. DNA vaccination against virus infection and enhancement of antiviral immunity following consecutive immunization with DNA and viral vectors. Ramsay A J; Leong K H; Ramshaw I A. (Division of Immunology and Cell Biology, John Curtin School of Medical Research, Australian National University, Canberra, Australia.. Alistair.Ramsay@anu.edu.au) . IMMUNOLOGY AND CELL BIOLOGY, (1997 Aug) 75 (4) 382-8. Ref: 55. Journal code: 8706300. ISSN: 0818-9641. Pub. country: Australia. Language: English.

AB Recent demonstrations of the immunogenicity of antigens encoded in DNA plasmids following delivery by various routes have heralded a new era in vaccine development. In this article, we review progress in DNA-based antiviral immunoprophylaxis. Preclinical studies have already established the immunogenicity of DNA plasmids encoding protective antigens from a wide variety of viral pathogens and work published in recent months has raised real prospects of broadly protective DNA vaccination against infections with influenza virus and HIV. We also describe a consecutive immunization protocol consisting of a priming dose of vaccine antigen encoded in DNA plasmids followed by a booster with the same antigen encoded in recombinant fowlpox virus vectors. We have used this strategy to generate protective antiviral cell-mediated immunity and sustained, high-level antibody responses both systemically and at mucosae, and to elucidate immunological mechanisms underlying the development of immunity to antigens delivered in DNA vectors.

L7 ANSWER 4 OF 29 MEDLINE on STN
97433405 Document Number: 97433405. PubMed ID: 9287173. Recombinant viruses as vaccines and immunological tools. Rolph M S; Ramshaw I A. (Department of Immunology, Max Planck Institute for Infection Biology, Monbijoustrasse 2, D-10117, Berlin, Germany.. rolph@mpiib-berlin.mpg.de) . CURRENT OPINION IN IMMUNOLOGY, (1997 Aug) 9 (4) 517-24. Ref: 85. Journal code: 8900118. ISSN: 0952-7915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Recombinant viruses have been investigated as candidate vaccines, and have also been used extensively as immunological tools. Recent advances in

this area include the following: the construction and testing of a recombinant simian immunodeficiency virus encoding human interferon-gamma; the development of new vectors such as recombinant poliovirus; and the generation of polyepitope vaccines. Basic immunological research has benefited from the use of recombinant viruses to further understand the role of molecules such as CD40 ligand, nitric oxide and interleukin-4.

L7 ANSWER 8 OF 29 MEDLINE on STN
96386606 Document Number: 96386606. PubMed ID: 8794356. Interleukin-4 mediates down regulation of antiviral cytokine expression and cytotoxic T-lymphocyte responses and exacerbates vaccinia virus infection in vivo. Sharma D P; Ramsay A J; Maguire D J; Rolph M S; Ramshaw I A. (Viral Engineering and Cytokine Research Group, John Curtin School of Medical Research, Australian National University, Canberra, Australia.) JOURNAL OF VIROLOGY, (1996 Oct) 70 (10) 7103-7. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Interleukin-4 (IL-4) promotes the growth of Th2-type cells while down regulating the development of Th1-type cells. It has been suggested that the actions of this factor inhibit Th1-type effector activity in vivo and may underlie the development of diseases normally controlled by cell-mediated immune responses. Here, we show that clearance of recombinant vaccinia viruses (VV) engineered to express the gene for murine IL-4 is markedly delayed in mice compared with control recombinant VV. While antiviral antibody levels and NK activity in mice given control virus or IL-4-expressing virus were similar, antiviral cytotoxic T-lymphocyte responses were profoundly suppressed throughout the course of infection with the latter. Limiting dilution analysis of IL-4-virus-infected spleens revealed a marked reduction in numbers of cytotoxic T-lymphocyte precursors. Furthermore, reverse transcriptase PCR analysis of splenic mRNA prepared from mice infected with the IL-4-expressing VV showed a marked down regulation of IL-12, gamma interferon, and IL-2 gene expression compared with that from mice given control virus. IL-4 also inhibited the production of nitric oxide (NO), a potent mediator of antimicrobial activity. Together, these data show that IL-4 markedly suppresses the development of antiviral cell-mediated immune responses in vivo with deleterious effects on virus clearance.

L7 ANSWER 13 OF 29 MEDLINE on STN
95132853 Document Number: 95132853. PubMed ID: 7831487. Enhancement of mucosal IgA responses by interleukins 5 and 6 encoded in recombinant vaccine vectors. Ramsay A J; Leong K H; Boyle D; Ruby J; Ramshaw I A. (Viral Engineering and Cytokine Research Group, John Curtin School of Medical Research, Australian National University, Canberra.) REPRODUCTION, FERTILITY, AND DEVELOPMENT, (1994) 6 (3) 389-92. Journal code: 8907465. ISSN: 1031-3613. Pub. country: Australia. Language: English.

AB **The expression of the genes for murine interleukin-5 (IL-5) or IL-6 in recombinant vaccinia virus vectors markedly increased IgA reactivity to co-expressed heterologous antigen in the lungs of mice inoculated intranasally with the viruses.** These elevated local IgA responses reached a peak four times higher than those elicited by control viruses 14 days after infection and these peak levels were maintained for at least four weeks. Elevated IgA responses, reaching a peak 3-4 weeks after immunization, were also observed in the lungs of mice inoculated with IL-6 expressed by another vector, fowlpox virus. The results

indicate that these factors enhance the development of mucosal IgA reactivity in vivo and suggest that their expression in mucosal vaccine vectors may stimulate local immune responses. The approach described in this study may be useful in stimulating mucosal immunity to a wide range of vector-encoded antigens, not only for vaccination against disease but also for immunocontraception by the co-expression of antigens involved in reproduction.

L7 ANSWER 14 OF 29 MEDLINE on STN
95132852 Document Number: 95132852. PubMed ID: 7831486. Cytokine regulation of mucosal responses: a rational basis for new vaccine delivery strategies. Husband A J; Bao S; Muir W; Ramsay A J; Ramshaw I A. (Department of Veterinary Pathology, University of Sydney, NSW, Australia.) REPRODUCTION, FERTILITY, AND DEVELOPMENT, (1994) 6 (3) 381-8. Ref: 68. Journal code: 8907465. ISSN: 1031-3613. Pub. country: Australia. Language: English.

AB In this review, cytokine regulation of mucosal responses is discussed in relation to the mucosal immune network and regulation of IgA responses. Based on this understanding, aspects of gene therapy for manipulation of the host environment and vaccine delivery systems are discussed. Although evidence obtained in vitro is briefly reviewed the general focus of this article is on evidence obtained from models in vivo.

L7 ANSWER 15 OF 29 MEDLINE on STN
95125394 Document Number: 95125394. PubMed ID: 7824886. Cytokines and murine autoimmune encephalomyelitis: inhibition or enhancement of disease with antibodies to select cytokines, or by delivery of exogenous cytokines using a recombinant vaccinia virus system. Willenborg D O; Fordham S A; Cowden W B; Ramshaw I A. (Neurosciences Research Unit, Woden Valley Hospital, Canberra, Australia.) SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1995 Jan) 41 (1) 31-41. Journal code: 0323767. ISSN: 0300-9475. Pub. country: ENGLAND: United Kingdom. Language: English.

AB To examine the complex role of cytokines in the pathogenesis of actively induced murine EAE we measured the levels of a number of cytokines (IL-6, IFN gamma and TNF) in the spinal cord and CSF of mice with active experimental autoimmune encephalomyelitis (EAE) and found them all to be elevated. We next treated mice with antibodies to these three cytokines, which were over expressed in the CNS, to determine if they would alter disease and found the following: anti-IL-6 had no significant effect on disease, anti-IFN gamma exacerbated disease, and anti-TNF either enhanced, had no effect or inhibited EAE depending on the antibody used. We then treated mice with exogenous cytokines , delivered using a recombinant vaccinia virus system, and found that the IL-6 and TNF virus constructs inhibited EAE whereas the IFN gamma construct had no effect on disease. Other cytokine recombinant viruses were also tested and it was found that the IL-1 beta, IL-2 and IL-10 viruses inhibited EAE while an IL-4 virus either had no effect or enhanced disease. We do not know the mechanism of action of the various cytokines in this system, but irrespective of the mechanism(s), this work clearly demonstrates that delivery of select cytokines using recombinant virus-cytokine constructs can provide a powerful means of down-regulating experimental organ-specific autoimmune disease.

L7 ANSWER 20 OF 29 MEDLINE on STN
93270672 Document Number: 93270672. PubMed ID: 8499074. A case for cytokines as effector molecules in the resolution of virus infection. Ramsay A J; Ruby J; Ramshaw I A. (John Curtin School

of Medical Research, Australian National University, Canberra, ACT.) IMMUNOLOGY TODAY, (1993 Apr) 14 (4) 155-7. Journal code: 8008346. ISSN: 0167-5699. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Some cytokines are known to have potent antiviral activity in vitro, and recent work shows that severely immunodeficient mice, which lack conventional effector T cells, can still recover from virus infection provided these factors are present at sites of virus replication. Here Alistair Ramsay, Janet Ruby and Ian Ramshaw discuss these findings and raise fundamental questions concerning the physiological role of cytotoxic T cells in the resolution of virus infection.

L7 ANSWER 21 OF 29 MEDLINE on STN
93143897 Document Number: 93143897. PubMed ID: 1369132. Cytokine expression by recombinant viruses--a new vaccine strategy. Ramshaw I A; Ruby J; Ramsay A. (Viral Engineering Group, John Curtin School of Medical Research, Australian National University.) TRENDS IN BIOTECHNOLOGY, (1992 Dec) 10 (12) 424-6. Journal code: 8310903. ISSN: 0167-7799. Pub. country: ENGLAND: United Kingdom. Language: English.

L23 ANSWER 1 OF 2 MEDLINE on STN
2001323774 Document Number: 20536036. PubMed ID: 11085586. Induction of HIV-1-specific T-helper responses and type 1 cytokine secretion following therapeutic vaccination of macaques with a recombinant fowlpoxvirus co-expressing interferon-gamma. Dale C J; Zhao A; Jones S L; Boyle D B; Ramshaw I A; Kent S J. (AIDS Pathogenesis Research Unit, Macfarlane Burnet Centre for Medical Research, Fairfield, Victoria, Australia.) JOURNAL OF MEDICAL PRIMATOLOGY, (2000 Aug) 29 (3-4) 240-7. Journal code: 0320626. ISSN: 0047-2565. Pub. country: Denmark. Language: English.

AB Preventive and/or therapeutic vaccines against Human Immunodeficiency Virus (HIV-1) are urgently required. Induction of cellular immunity is favoured since these responses correlate with control of HIV-1. Recombinant fowlpoxvirus (FPV) vaccines encoding both HIV-1 gag/pol and interferon-gamma (FPV gag /pol-IFNgamma) were hypothesised to enhance HIV -specific cellular immunity and were further evaluated in macaques previously infected with HIV-1. A novel assay to detect IFNgamma secretion following HIV antigen stimulation of whole blood was developed to further assess the safety and immunogenicity of the FPV gag/pol-IFNgamma vaccine. Immunisation with FPV gag/pol-IFNgamma safely enhanced HIV-specific IFNgamma secretion following ex vivo stimulation of whole blood, greater than that observed following FPV gag/pol vaccination not co-expressing IFNgamma. Both HIV-specific IFNgamma-spot-forming cells by ELISPOT and CD69 expression by CD4+ lymphocytes were also enhanced following FPV gag/pol-IFNgamma vaccination. Hence, the FPV-HIV vaccine co-expressing IFNgamma stimulated HIV -specific T cell responses in macaques, and should be further evaluated as a therapeutic or preventive HIV vaccine.

L23 ANSWER 2 OF 2 MEDLINE on STN
2000184014 Document Number: 20184014. PubMed ID: 10717345. A recombinant avipoxvirus HIV-1 vaccine expressing interferon-gamma is safe and immunogenic in macaques. Kent S J; Zhao A; Dale C J; Land S; Boyle D B; Ramshaw I A. (AIDS Pathogenesis Research Unit, Macfarlane Burnet Centre for Medical Research, Yarra Bend Rd, Fairfield, Australia..

kent@burnet.edu.au) . VACCINE, (2000 Apr 28) 18 (21) 2250-6. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Complex recombinant fowlpoxvirus (rFPV) vaccines expressing both HIV-1 antigens and type 1 cytokines could facilitate the induction of cellular immunity against HIV-1. A single rFPV expressing both HIV-1gag/pol and human interferon-gamma (FPVgag/pol-IFNgamma) was constructed and assessed as a therapeutic vaccine for safety and immunogenicity in macaques (Macaca nemestrina) previously infected with HIV-1. FPV gag/pol-IFNgamma vaccinations were safe and enhanced T cell proliferative responses to Gag antigens (but not control tetanus antigens). Enhanced CTL responses to gag/pol antigens were also observed following IFNgamma expressing vaccinations. Since cellular immunity may be critical to controlling or preventing HIV-1 infection, these observations suggest that avipox vectors co-expressing IFNgamma should be further evaluated as therapeutic or preventive HIV-1 vaccines.

L4 ANSWER 18 OF 46 MEDLINE on STN
97288401 Document Number: 97288401. PubMed ID: 9143379. Strong augment effect of IL-12 expression plasmid on the induction of HIV-specific cytotoxic T lymphocyte activity by a peptide vaccine candidate. Hamajima K; Fukushima J; Bukawa H; Kaneko T; Tsuji T; Asakura Y; Sasaki S; Xin K Q; Okuda K. (Department of Bacteriology, Yokohama City University School of Medicine, Japan.) CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1997 May) 83 (2) 179-84. Journal code: 0356637. ISSN: 0090-1229. Pub. country: United States. Language: English.

AB We previously reported that repeated inoculation of VC1, a macromolecular multicomponent peptide vaccine emulsified with Freund's adjuvant (VC1-F), induced high cytotoxic T lymphocyte (CTL) levels and a substantial level of multivalent antibodies which neutralized various human immunodeficiency virus type 1 (HIV-1) isolates. In the present study, we report that inoculation of VC1-F plus interleukin (IL)-12 expression plasmid can induce a higher antigen-specific CTL response compared to that with VC1-F alone. VC1-F plus IL-12 expression plasmid or VC1-F alone were inoculated to BALB/c mice twice at interval of 2 weeks. Two weeks after the second inoculation, spleen effector cells from these mice were examined. **Stronger CTL responses against target cells were observed from the inoculation of VC1-F plus IL-12 plasmid than from that with VC-1F alone,** but there was no difference in antibody induction. The inoculation of VC1 plus IL-12 plasmid also produced higher CTL activity than the inoculation of VC1 alone. These augmented CTL activities were not observed using target cells pulsed with non-HIV-specific peptides and different class I haplotype cells. These data demonstrate that **co-inoculation of cell-mediated immune potent antigen and IL-12 plasmids can enhance the antigen-specific CTL response**. This may be a potential approach for the induction of cellular immunization against HIV-1 and other diseases.

L4 ANSWER 3 OF 46 MEDLINE on STN
1998375874 Document Number: 98375874. PubMed ID: 9712056. Augmentation and suppression of immune responses to an HIV-1 DNA vaccine by plasmid cytokine/Ig administration. Barouch D H; Santra S; Steenbeke T D; Zheng X X; Perry H C; Davies M E; Freed D C; Craiu A; Strom T B; Shiver J W; Letvin N L. (Division of Viral Pathogenesis, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA 02215,

USA.) JOURNAL OF IMMUNOLOGY, (1998 Aug 15) 161 (4) 1875-82. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The use of cytokines has shown promise as an approach for amplifying vaccine-elicited immune responses, but the application of these immunomodulatory molecules in this setting has not been systematically explored. In this report we investigate the use of protein- and plasmid-based cytokines to augment immune responses elicited by an HIV-1 gp120 plasmid DNA vaccine (pV1J-gp120) in mice. **We demonstrate that immune responses elicited by pV1J-gp120 can be either augmented or suppressed by administration of plasmid cytokines. A dicistronic plasmid expressing both gp120 and IL-2 induced a surprisingly weaker gp120-specific immune response than did the monocistronic pV1J-gp120 plasmid. In contrast, systemic delivery of soluble IL-2/Ig fusion protein following pV1J-gp120 vaccination significantly amplified the gp120-specific immune response as measured by Ab, proliferative, and CTL levels.** Administration of plasmid IL-2/Ig had different effects on the DNA vaccine-elicited immune response that depended on the temporal relationship between Ag and cytokine delivery. Injection of plasmid IL-2/Ig either before or coincident with pV1J-gp120 suppressed the gp120-specific immune response, whereas injection of plasmid IL-2/Ig after pV1J-gp120 amplified this immune response. To maximize immune responses elicited by a DNA vaccine, therefore, it appears that the immune system should first be primed with a specific Ag and then amplified with cytokines. The data also show that IL-2/Ig is more effective than native IL-2 as a DNA vaccine adjuvant.

L4 ANSWER 34 OF 46 MEDLINE on STN
95012932 Document Number: 95012932. PubMed ID: 7927981. AIDS vaccines and adjuvant formulations. Cernescu C E. (St. Nicolau Institute of Virology, Bucharest, Romania.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (1994 May-Jun) 16 (5-6) 369-79. Ref: 54. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The AIDS epidemic is too large to continue ignoring prevention programs that appear to work. In this review the promising experimental immunogens and how close they are to the optimal requirements for a preventive vaccine are presented. Adjuvants and adjuvant formulations (mainly mixtures of adjuvants with suitable vehicles) can help in solving some specific problems of AIDS vaccines: overcome the variable nature of HIV subtypes, generate both antibody and T-cell response, induce mucosal immunity, avoid enhancing or autoimmune antibodies and distinguish vaccine-induced seropositivity from natural HIV infection. The following categories of adjuvants are discussed: alum, other mineral and bacterial cell-wall derived adjuvants, cytokines, carriers and vehicles. **Although many specific mechanisms of the relative effectiveness of adjuvants have been clarified by recent advances in basic immunology the best adjuvant formulation remains largely empirical.** A standardized protocol for preclinical testing of adjuvants for AIDS vaccines is a priority task.

L4 ANSWER 32 OF 46 MEDLINE on STN
95105072 Document Number: 95105072. PubMed ID: 7806429. T-cell adjuvants. Hadden J W. (Department of Internal Medicine, University of South Florida Medical College, Tampa 33612.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (1994 Sep) 16 (9) 703-10. Ref: 81. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom.

Language: English.

AB T-cell adjuvancy involves the use of agents to stimulate preferentially delayed type hypersensitivity (DTH). Traditional adjuvants like Alum, Freunds, muramyl peptides, and endotoxins are not selective. Natural infection (e.g. vaccinia) may yield selective DTH. Low dose cyclophosphamide (CY) with mycobacteria was the first experimental T-cell adjuvant. New adjuvant formulations (ISCOMS, MAPS, etc.) with synthetic T-cell epitopes offer improved formulations. Upregulation of TH-1 helper cells and their actions with interleukins like IL-2, IL-12, and gamma IFN or antibodies to IL-4 and IL-10 may augment potently pathogen and tumor resistance. Similarly, transfection of tumor target cells with genes for IL-2, IL-12, gamma IFN, etc., offers novel vaccine treatment approaches. Finally, "thymomimetic" peptides like thymosin alpha 1 or drugs like levamisole or isoprinosine alone or in conjunction with interleukins may augment TH-1 and DTH responses. These approaches are seeing increasing emphasis in new treatment strategies for cancer and infections like HIV.

L10 ANSWER 12 OF 108 MEDLINE on STN
1998320553 Document Number: 98320553. PubMed ID: 9656448. Cytokine adjuvants: lessons from the past--guidelines for the future?. Hughes H P. (Mallinckrodt Veterinary, Mundelein, IL 60060, USA.) VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1998 May 15) 63 (1-2) 131-8. Ref: 22. Journal code: 8002006. ISSN: 0165-2427. Pub. country: Netherlands. Language: English.

AB Formulation of vaccines has for the most part relied on simple adjuvants which are able to enhance the immune response to the immunogen. Cytokines are an attractive alternative to conventional preparations, and have been tested in a number of different systems. However, **experience has indicated that there are a number of guidelines that must be followed. The dose of cytokine administered is critical for optimal effect. Too little will have no effect, and too much will have undesirable side effects. For instance, at high doses IL-2 can induce autoimmune disease and interferon gamma can have a suppressive effect.** Cytokines may also have to be administered at the same site or even to the same cell as the antigen for optimal effect. Conjugation or molecular chimerization of antigens and cytokines can achieve this effect efficiently. Formulation of cytokine with antigen may overcome any detrimental effect that the antigen may have. Should the antigen have any suppressive epitopes or have a direct effect on essential intracellular mechanisms, cytokines may be used to overcome these effects. In some cases, Th1 or Th2 cytokines have been used to enhance a protective Th1 or Th2 response. However, the paradigm does not always hold, and Th1 cytokines can enhance Th2 responses, or have no overall effect on phenotype. Further, in some host species, there is evidence that there may be no Th1/Th2 dichotomy. The most important aspect of using cytokines as adjuvants is in ensuring that there is a balanced response.

L14 ANSWER 16 OF 25 MEDLINE on STN
2000059061 Document Number: 20059061. PubMed ID: 10593488. Antigen-specific humoral and cellular immune responses can be modulated in rhesus macaques through the use of IFN-gamma, IL-12, or IL-18 gene adjuvants. Kim J J; Nottingham L K; Tsai A; Lee D J; Maguire H C; Oh J; Dentchev T; Manson K H; Wyand M S; Agadjanyan M G; Ugen K E; Weiner D B. (Department of Pathology, University of Pennsylvania, Philadelphia 19104, USA.) JOURNAL OF MEDICAL PRIMATOLOGY, (1999 Aug-Oct) 28 (4-5) 214-23. Journal code: 0320626. ISSN: 0047-2565. Pub. country: Denmark. Language:

English.

AB DNA or nucleic acid immunization has been shown to induce both antigen-specific cellular and humoral immune responses in vivo. Moreover, immune responses induced by DNA immunization can be enhanced and modulated by the use of molecular adjuvants. To engineer the immune response in vivo towards more T-helper (Th)1-type cellular responses, we investigated the co-delivery of inteferon (IFN)-gamma, interleukin (IL)-12, and IL-18 genes along with DNA vaccine constructs. We observed that both antigen-specific humoral and cellular immune responses can be modulated through the use of cytokine adjuvants in mice. Most of this work has been performed in rodent models. There has been little confirmation of this technology in primates. We also evaluated the immunomodulatory effects of this approach in rhesus macaques, since non-human primates represent the most relevant animal models for human immunodeficiency virus (HIV) vaccine studies. As in the murine studies, **we also observed that each Th1 cytokine adjuvant distinctively regulated the level of immune responses generated. Co-immunization of IFN-gamma and IL-18 in macaques enhanced the level of antigen-specific antibody responses**. Similarly, co-delivery of IL-12 and IL-18 also enhanced the level of antigen-specific Th proliferative responses. These results extend this adjuvant strategy in a more relevant primate model and support the potential utility of these molecular adjuvants in DNA vaccine regimens.